

THE AN GROUP

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May 13, 2005

BEHQ-0505-16034

U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
EPA East Building, Room 6428
1201 Constitution Avenue, NW
Washington, DC 20004
Attention: 8(e)

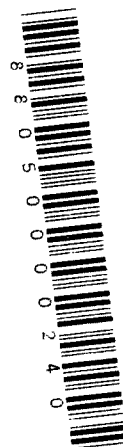
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Dear TSCA 8(e) Coordinator:

On behalf of the The Acrylonitrile Group (AN Group) and its members¹, I am writing to notify the Agency of preliminary information regarding irritation effects observed in the nasal tissues of male and female rats exposed to acrylonitrile (AN). These observations were made as part of a two-generation inhalation toxicology study being sponsored by the AN Group².

In this study, F₀ males and females were exposed for six hours per day, seven days per week, for a minimum of 70 days prior to mating. Exposure of F₀ males was continuous until termination at the weaning of their offspring. Exposure of the F₀ females continued throughout mating until gestation day 20. To avoid confounding effects on nesting and nursing behavior, exposure for the F₀ dams was suspended from gestation day 21 through lactation day 4; exposures were re-initiated on lactation day 5. This means that the F₁ and F₂ generations were potentially exposed to the test article *in utero*, through nursing, and then via inhalation starting on day 28.

Four levels of the nasal cavity were examined microscopically in the control, 5, 15 and 45 ppm dose groups. Morphologic changes in the respiratory epithelium were present in Level I in the F₀ males and females in the 45 ppm group, in the F₁ males at exposure concentrations of 5, 15 and 45 ppm and in the F₁ females at exposure concentrations of 15 and 45 ppm. The severity of the changes increased with increasing vapor concentration and included respiratory/ transitional epithelial hyperplasia, subacute inflammation, and squamous metaplasia. The response seen in the lower dose groups in the F₁ generation suggests age-related morphometric differences between the F₁ animals (28 days at initial exposure) and the F₀ animals (approximately 8 weeks at initial exposure). In addition to the changes in the respiratory epithelium, olfactory epithelial degeneration in the dorsal meatus was observed in F₀ and F₁ males and females exposed to 45 ppm.

¹ Members of the AN Group include: Cytec Industries; The Dow Chemical Company; E.I. du Pont de Nemours and Company; GE Advanced Materials - Plastics; Innovene; and Lanxess Corporation.

² As part of its October 14, 2003 submission to the IRIS Desk, the AN Group notified the Agency of its plans to conduct this multi-generation reproduction study.

MR 286330

Office of Pollution Prevention and Toxics

May 13, 2005

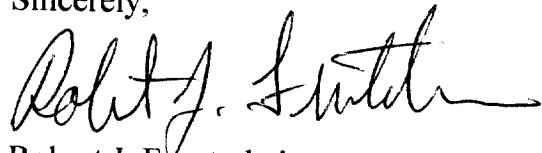
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According to the study pathologist, the majority of the respiratory lesions in the nasal tissues were present in the most anterior section examined. The nasal lesions observed were consistent with those expected from a local irritant, which are typically reversible upon cessation of exposure and do not suggest a systemic effect targeted at the nasal tissues. Actual recovery from the nasal effects in this study could not be evaluated since the study design for evaluation of potential reproductive toxicity required continuous (7-day/week) exposure to AN.

Knowledge that AN is an irritant has long been recognized. As noted in EPA's Air Toxics Hazard Summary for acrylonitrile, workers exposed via inhalation to high levels of AN have experienced mucous membrane irritation (<http://www.epa.gov/ttn/atw/hlthef/acryloni.html>). Nonetheless, the AN Group decided that it would be prudent to submit this information at this time. We will provide a full copy of the final report when it becomes available.

Please do not hesitate to contact me if we can provide any further information.

Sincerely,

A handwritten signature in black ink, appearing to read "Robert J. Fensterheim", with a long horizontal flourish extending to the right.

Robert J. Fensterheim
Executive Director